selected from the group consisting of GFP, colloidal gold, streptavidin, avidin and biotin.

REMARKS/ARGUMENTS

Claims 1-10 remain in this application. No claims have been added.

In response to the Office Action of December 17, 2002, Applicants request re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Elections/Restrictions

This application has been deemed to contain claims directed to the following patentably distinct species of the claimed invention: species of interactive mapping steps listed in claims 6 and 9: 1) creation of engineered antibodies, 2) directly determining the three dimensional structure of said antibody directly from an amino acid sequence thereof, 3) cellular localization, 4) sub-cellular localization, 5) protein-protein interaction, 6) receptor-ligand interaction, and 7) pathway delineation. Claims 7 and 10 are drawn to species 1.

Applicant has been required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-5, and 8

are generic.

During a telephone conversation with Ferris Lander on 09 December 2002, a provisional election was made with traverse to prosecute the invention of species 1, claims 1-10.

Applicant hereby affirms this election.

Specification

It has been brought to the Applicant's attention that the appendix attached to the application at the time of filing is not deemed to be a part of the specification and will not be published should the instant application issue as a patent. The appendix was not included in the numbered pages of the specification, and was not indicated to be part of the specification in the transmission papers at the time of filing.

The disclosure is therefore objected to because of the following informalities: On page 32, line 15, the specification refers to an Appendix A that is not part of the specification.

During a teleconference with Examiner Brusca on June 17, 2003, it was determined that filing of a new Declaration which includes mention of the Appendix, and subsequent renumbering of the Appendix to include it as part of the specification would be an acceptable way of eliminating the

objection to the disclosure. This will be carried out in due course, and forwarded as a separate paper.

Rejections under 35 USC 102(e)

Claim 1 stands rejected under 35 U.S.C. 102(e) as being anticipated by Hutchens et al.

The claim is deemed to be drawn to a method of isolating a protein sample from a patient, comparing the protein sample to a proteomic database, and determining whether the proteomic sample is diagnostic of a disease.

Hutchens et al. is alleged to show throughout a method of analysis of proteomic samples by use of retentate chromatography coupled with MALDI-TOF mass spectrometry analysis. Hutchens et al. is further alleged to show development of a diagnostic assay in columns 4 and 7, and is deemed to exemplify a diagnostic assay in Figures 21A-21D (normal versus diseased human serum analysis) and 23A-23D (human cancer patient urine analysis). Hutchens et al. is further alleged to show comparison to databases and data analysis in columns 34-36, and such database comparison in figures 21A-21D and 23A-23D. Hutchens et al. is alleged to show the development of diagnostic probes for use with proteomic samples in columns 40-41, and the development of diagnostic proteomic methods in columns 43-44, and as claimed

in claim 2, where development of differential expression analysis methods are discussed in the context of diagnostic markers.

Claim 1 has been amended to "consisting essentially of" to close the claim to any steps which would materially affect the novel characteristics of the invention. At the same time, the step of preparing said patient sample to facilitate proteomic investigation thereof has been amended to state the use of micro-chromatographic columns (see page 26 of the specification, 1.3 et seq.) which evidence a form of ***partition chromatography*** which is not retentate chromatography. Thus the reference to Hutchens et al can not anticipate the instantly claimed process as amended.

Rejection under 35 USC 103(a)

Claims 2, 3, 4, 5, and 8 and claim 1 from which they depend are deemed to be rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchens et al. in view of Jungblut et al. The claims are deemed to be drawn to a method of isolating a protein sample from a patient, comparing the protein sample to a proteomic database, and determining whether the proteomic sample is diagnostic of a disease. In some embodiments the method includes sequencing the proteomic sample, developing an antibody to the proteomic sample, expression of a protein to which the antibody is specific

for, and using an antibody to analyze a protein of the sample.

Hutchens et al. is deemed to show throughout a method of analysis of proteomic samples by use of retentate chromatography coupled with MALDI-TOF mass spectrometry analysis. Hutchens et al. is alleged to show development of a diagnostic assay in columns 4 and 7, and is further deemed to exemplify a diagnostic assay in figures 21A-21D (normal versus diseased human serum analysis) and 23A-23D (human cancer patient urine analysis). Hutchens et al. is further alleged to show a comparison to databases and data analysis in columns 34-36, and is deemed to exemplify such database comparison in Figures 21A-21D and 23A-23D. Hutchens et al. is alleged to show the development of diagnostic probes for use with proteomic samples in columns 40-41, and is further deemed to show development of diagnostic proteomic methods in columns 43-44, and as claimed in claim 2, where development of differential expression analysis methods are discussed in the context of diagnostic markers. Hutchens et al. does not show methods including sequencing the proteomic sample, developing an antibody to the proteomic sample, explicit expression of a protein to which the antibody is specific for, or using an antibody to analyze a protein of the sample.

Jungblut et al. is deemed to show proteomic analysis

methods for disease diagnosis throughout and especially in Figure 1. Jungblut et al. is indicated as showing sequencing of a protein in the sample for the purpose of identification matching in a database on page 2102. Jungblut et al. is further alleged to show use of antibodies for identification of a hepatocellular carcinoma related protein in figure 4 and page 2103, and for identification of heat shock proteins associated with dilated cardiomyopathy on page 2104. Regarding the limitation of expression of the protein in claim 4, both Hutchens et al. and Jungblut et al. are alleged to show use of proteins that were expressed in the patient before the sample was obtained.

Claims 6, 7, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchens et al. in view of Jungblut et al. as applied to claims 2, 3, 4, 5, and 8 and claim 1 from which they depend above, and further in view of Watkins.

The claims are drawn to proteomic diagnostic methods that use antibodies labeled with biotin or colloidal gold. Hutchens et al. in view of Jungblut et al. as applied to claims 2, 3, 4, 5, and 8 and claim 1 from which they depend above does not show antibodies labeled with biotin or colloidal gold. Watkins is cited for allegedly showing on pages 14.6.5-14.6.11 that antibodies labeled with biotin or

colloidal gold are useful for detecting antigens in histological samples.

The Examiner indicates that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Hutchens et al. in view of Jungblut et al. as applied to claims 2, 3, 4, 5, and 8 and claim 1 from which they depend above by use of the biotin or colloidal gold antibody labeling methods of Watkins because Watkins shows that such labeling methods allow of detection of antigens in histological samples.

It is respectfully submitted that this rejection must be withdrawn in view of the amendments to claim 1 and the arguments regarding Hutchens et al supra. The teaching away of the instant invention from any form of retentate chromatography (see specification at page 16, line 18 et seq) renders any combination of references with Hutchens et al inappropriate in promulgating a prima facie case of obviousness against the instantly presented claims. The skilled artisan would have no suggestion to abandon retentate chromatography as required by Hutchens et al, in favor of a partition chromatography type approach, utilizing micro-chromatographic columns, as illustrated and reduced to practice by the instant Applicants.

SUMMARY

In light of the foregoing remarks and amendment to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,

Ferris H. Lander

Ferris H. Lander
Registration # 43,377

McHale & Slavin, P.A.
4440 PGA Blvd., Suite 402
Palm Beach Gardens, FL 33402
(561) 625-6575 (Voice)
(561) 625-6572 (Fax)

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